**Validity of a Polygenic Risk Score for Predicting Type 1 Diabetes in a Diverse Australian Paediatric Cohort**

**Aim:** Polygenic risk scores for type 1 diabetes (T1D) have been proposed to identify children with an increased genetic risk, irrespective of their family history. This study aimed to assess the validity of using a T1D polygenic risk score, derived from a primarily-Caucasian population, in the rich, multiethnic Australian population.

**Method:** Deidentified purified DNA samples from children with T1D in the Australasian Diabetes Data Network (ADDN) biobank at the Children’s Hospital at Westmead, Sydney were included. Samples were analysed for 67 single nucleotide polymorphisms (SNPs) and individual T1D polygenic risk scores were calculated as the weighted sum of the risk associated with each SNP. T1D risk centiles were obtained from the corresponding scores in the UK Biobank. Demographics were extracted from the ADDN Biobank/medical records.

**Results:** 462 children were included in the analysis (51% male, mean age at T1D diagnosis was 7.5 ± 3.9 years). A third (35%) were non-Australian/European and almost a quarter (24%) reported 2 or more ethnicities. Overall, 42% were Australian, 39% European, 14% Middle Eastern, 8% South Asian, 8% East Asian, 5% Pacific Islander, 4% Aboriginal or Torres Strait Islander (ATSI), 3% African, 1% South American and 2% Other. Two-thirds of T1D cases (66%) were >90th centile by risk score and 80% were >80th centile. The T1D polygenic risk score was most accurate in children identifying as Australian (73% >90th centile), European (71%) or ATSI (70%) children and least accurate in African (38%) or South American (40%) children.

**Conclusion:** The T1D polygenic risk score is a valid tool for predicting children with T1D in a multiethnic population, with greatest accuracy for children from Australian and European descent. Genetic risk-stratification could improve the efficiency of a future T1D national screening program.